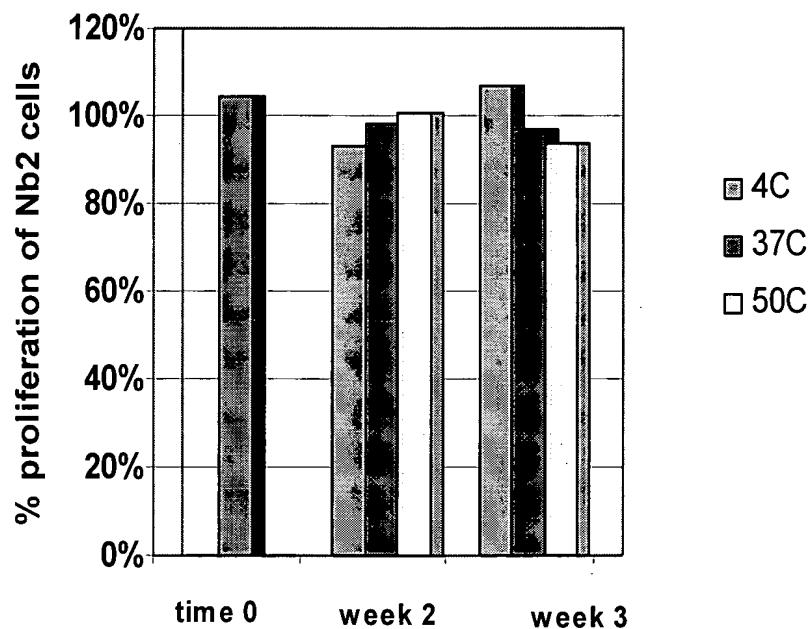
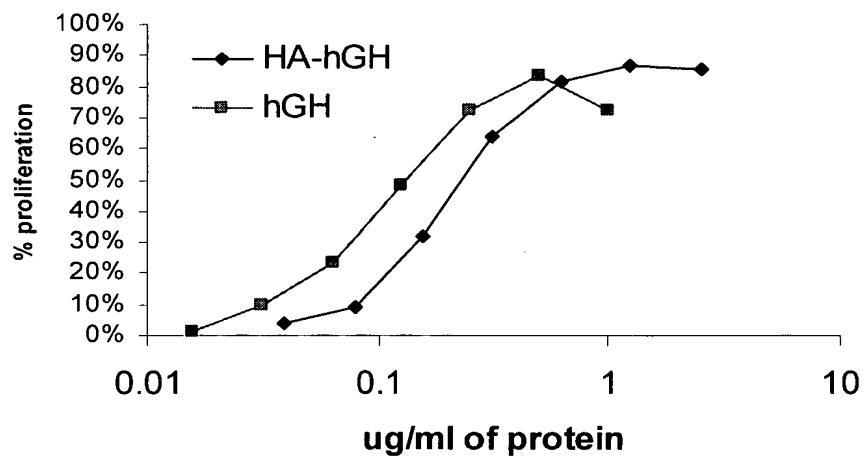


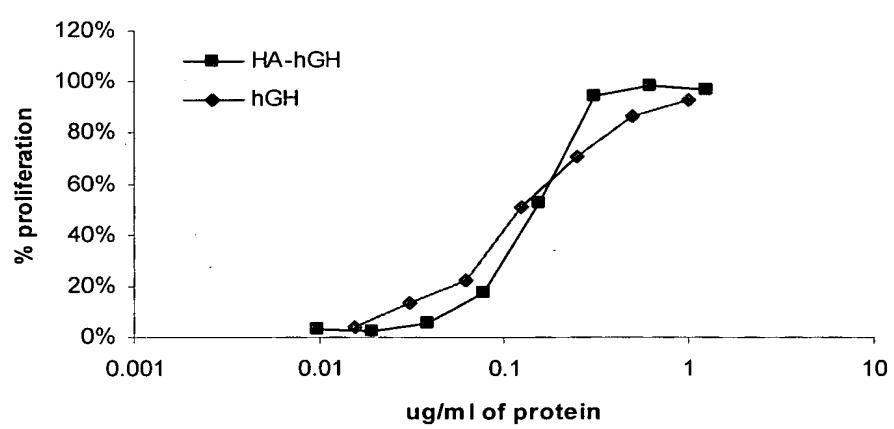
**Figure 1**



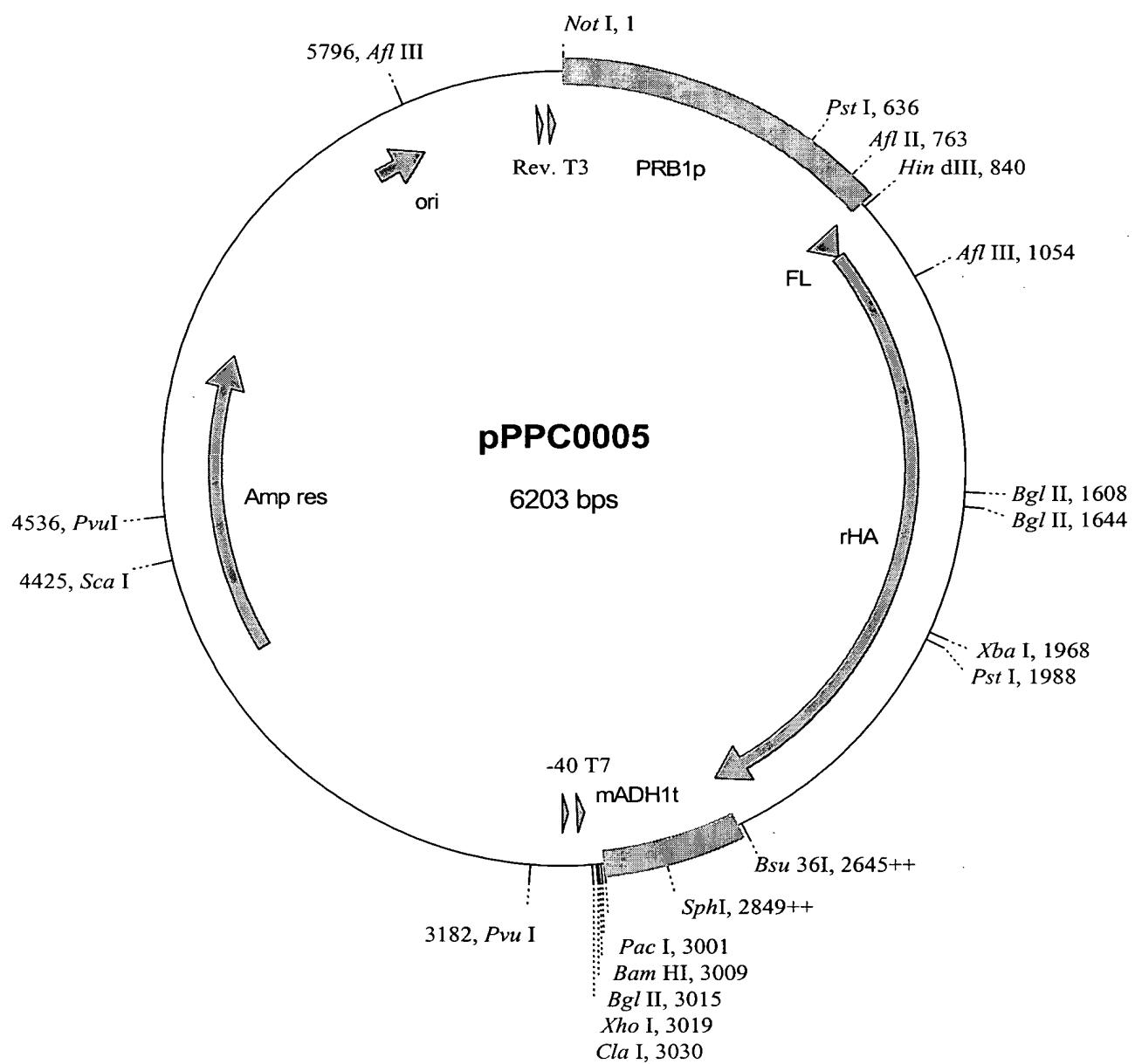
**Figure 2**



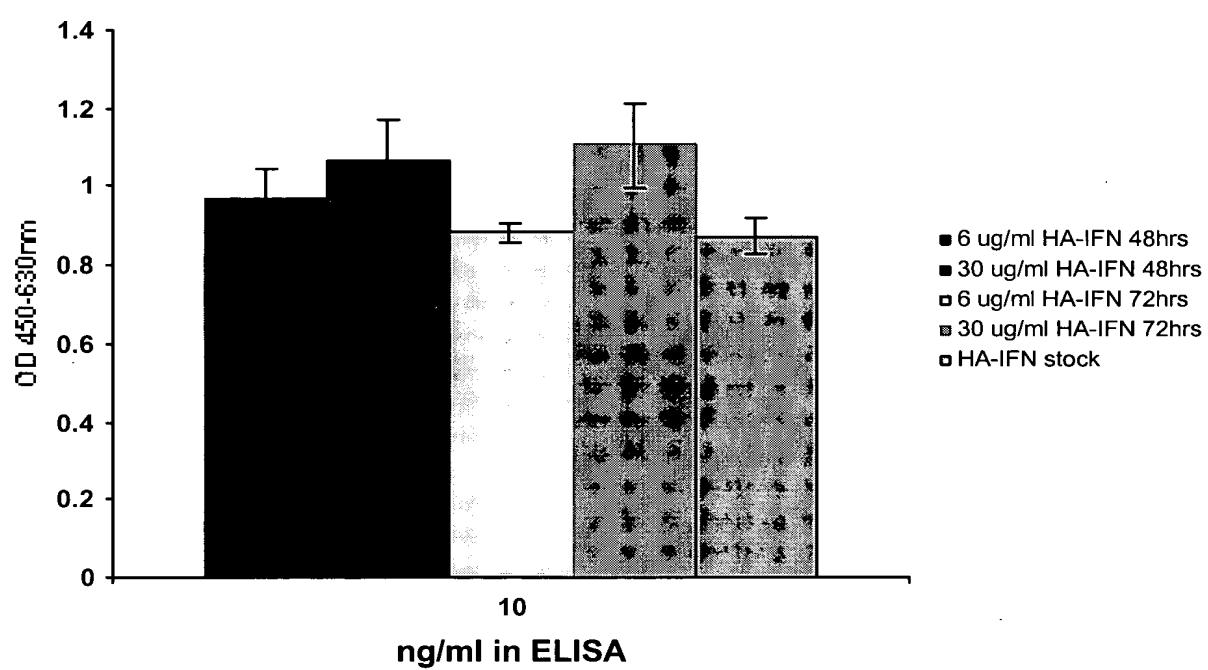
**Figure 3A**



**Figure 3B**



**Figure 4**



**Figure 5**

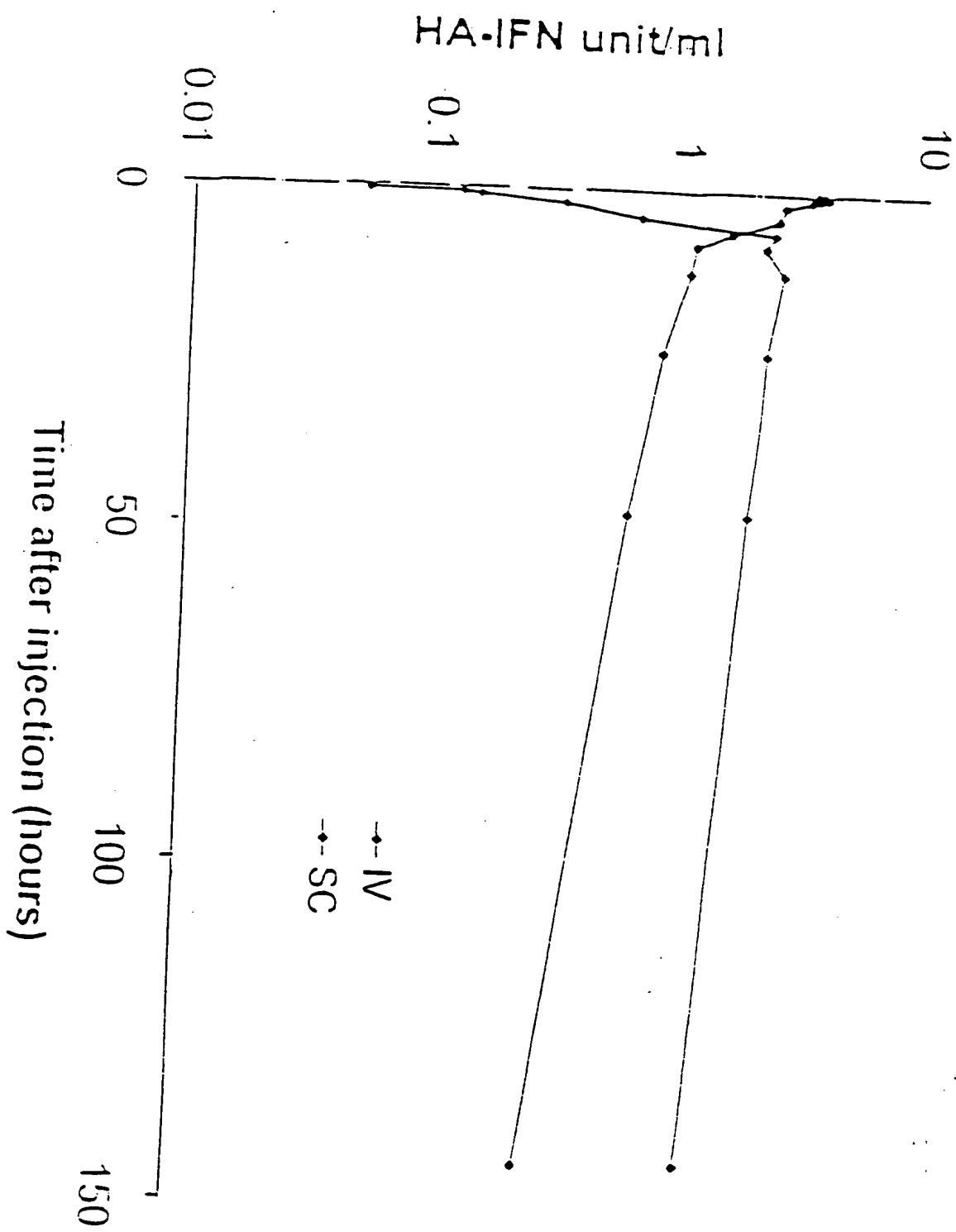
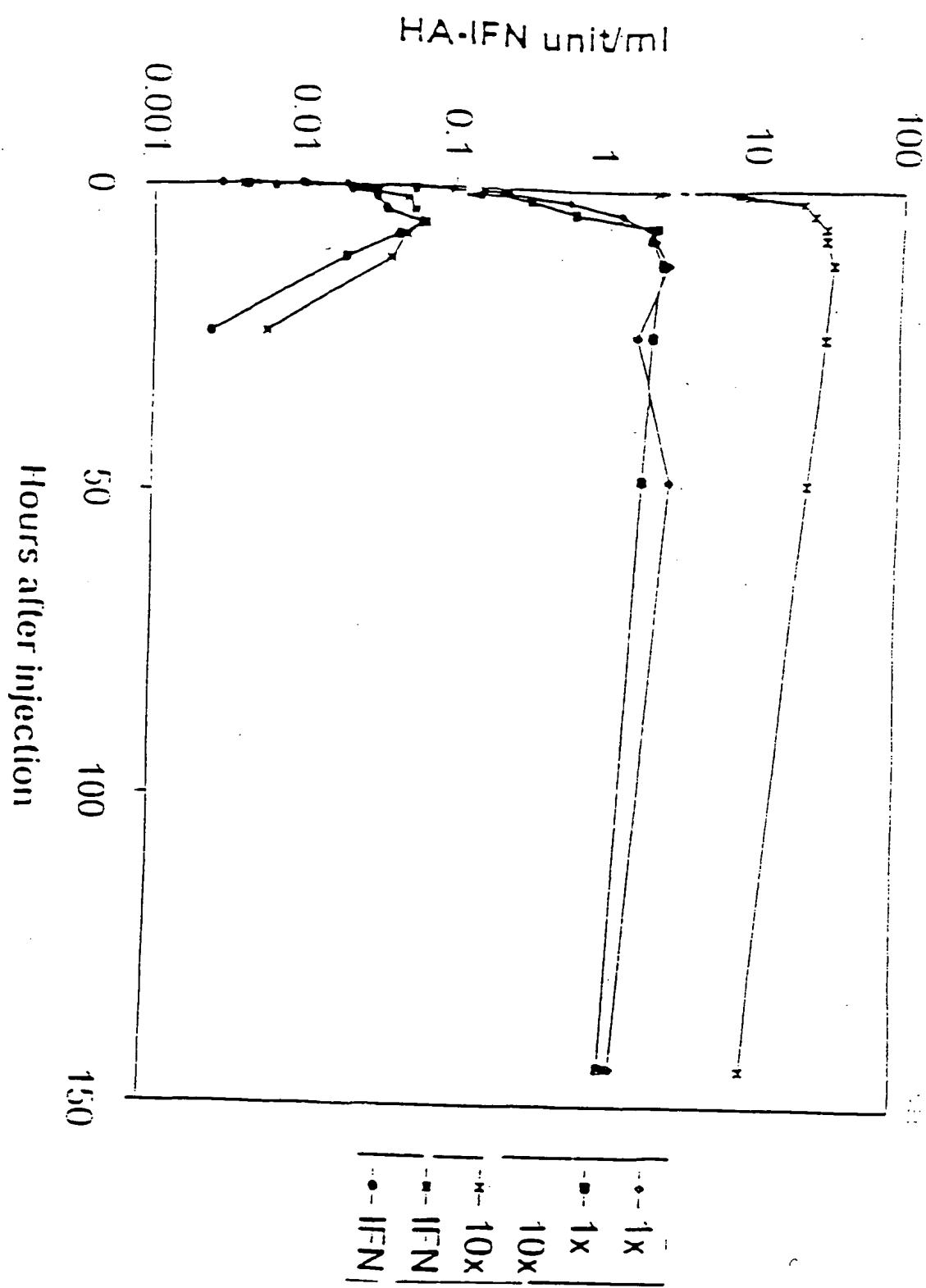


Figure 6



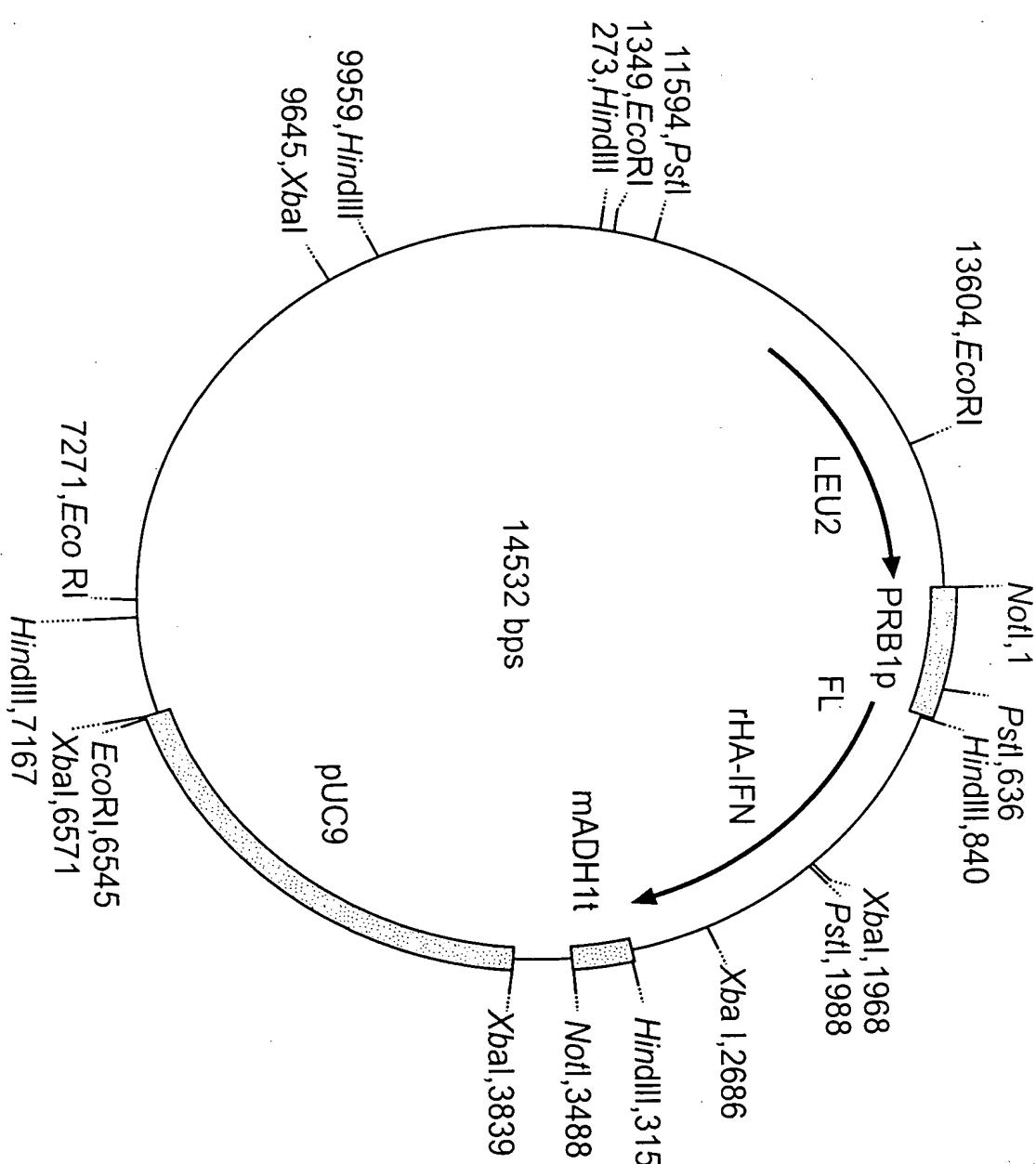


FIG.  
8

**Figure 9**

| <b>Loop</b> |               | <b>Loop</b> |               |
|-------------|---------------|-------------|---------------|
| I           | Val154-Asn61  | VII         | Glu280-His288 |
| II          | Thr76-Asp89   | VIII        | Ala362-Glu368 |
| III         | Ala92-Glu100  | IX          | Lys439-Pro447 |
| IV          | Gln170-Ala176 | X           | Val462-Lys475 |
| V           | His247-Glu252 | XI          | Thr478-Pro486 |
| VI          | Glu266-Glu277 | XII         | Lys560-Thr566 |

## Figure 10

### a. Randomisation of Loop IV.

151      APELLFFAKR YKAAFTECCQ AADKAACLLP KLDELRDEGK ASSAKQRLKC  
                  HHHHHHHHHHH HHHHHHHHHH                   HHHHH HHHHHHHHHHHH HHHHHHHHHHHH  
  
151      APELLFFAKR YKAAFTECCX XXXXXXCLLP KLDELRDEGK ASSAKQRLKC  
                  HHHHHHHHHHH HHHHHHHHHH                   HHHHH HHHHHHHHHHHH HHHHHHHHHHHH

**X** represents the mutation of the natural amino acid to any other amino acid. One, more or all of the amino acids can be changed in this manner. This figure indicates all the residues have been changed.

### b. Insertion (or replacement) of Randomised sequence into Loop IV.

(X)<sub>n</sub>  
↓  
151      APELLFFAKR YKAAFTECCQ AADKAACLLP KLDELRDEGK ASSAKQRLKC  
                  HHHHHHHHHHH HHHHHHHHHH                   HHHHH HHHHHHHHHHHH HHHHHHHHHHHH

The insertion can be at any point on the loop and a length where n would typically be 6, 8, 12, 20 or 25.

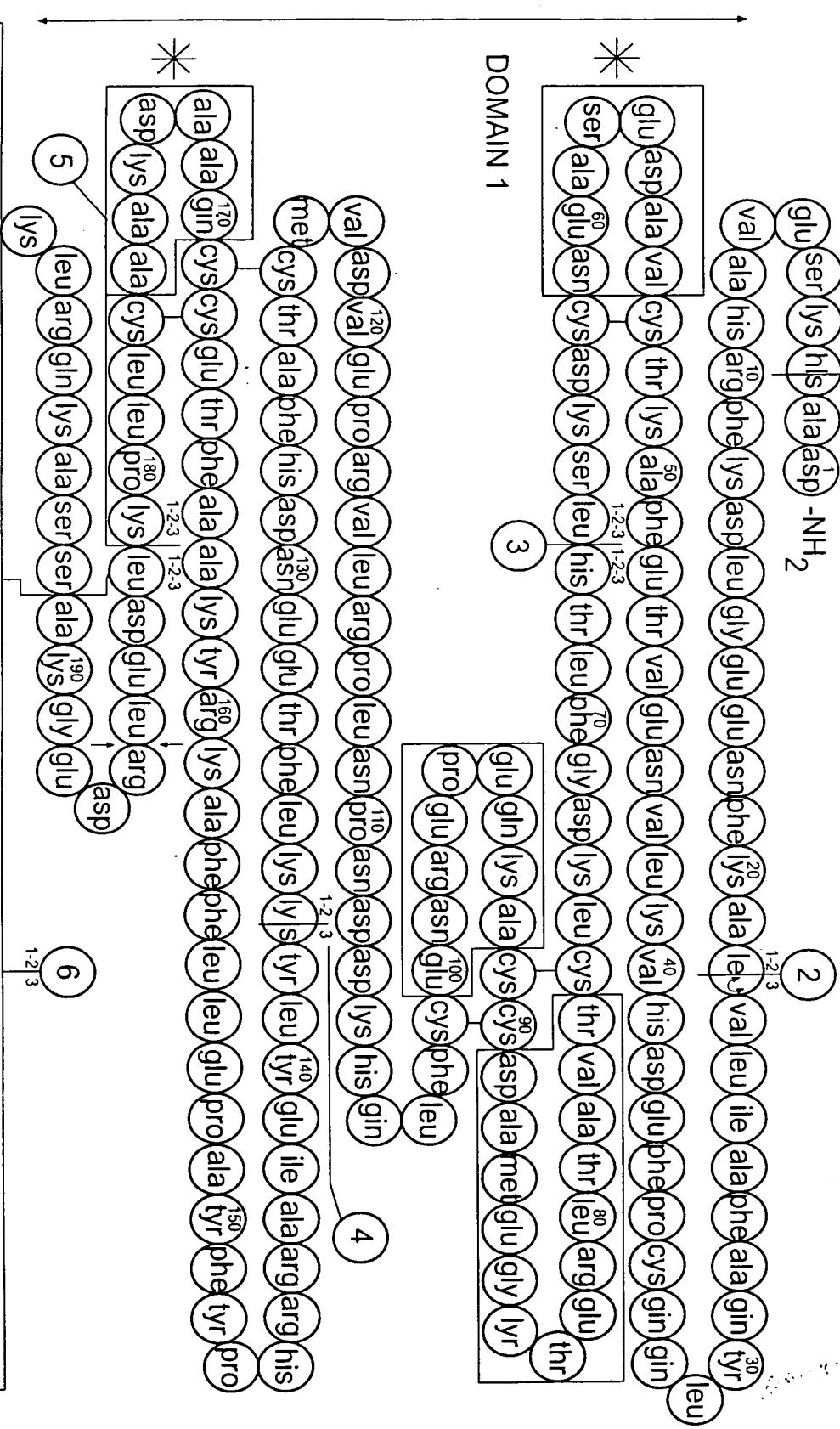
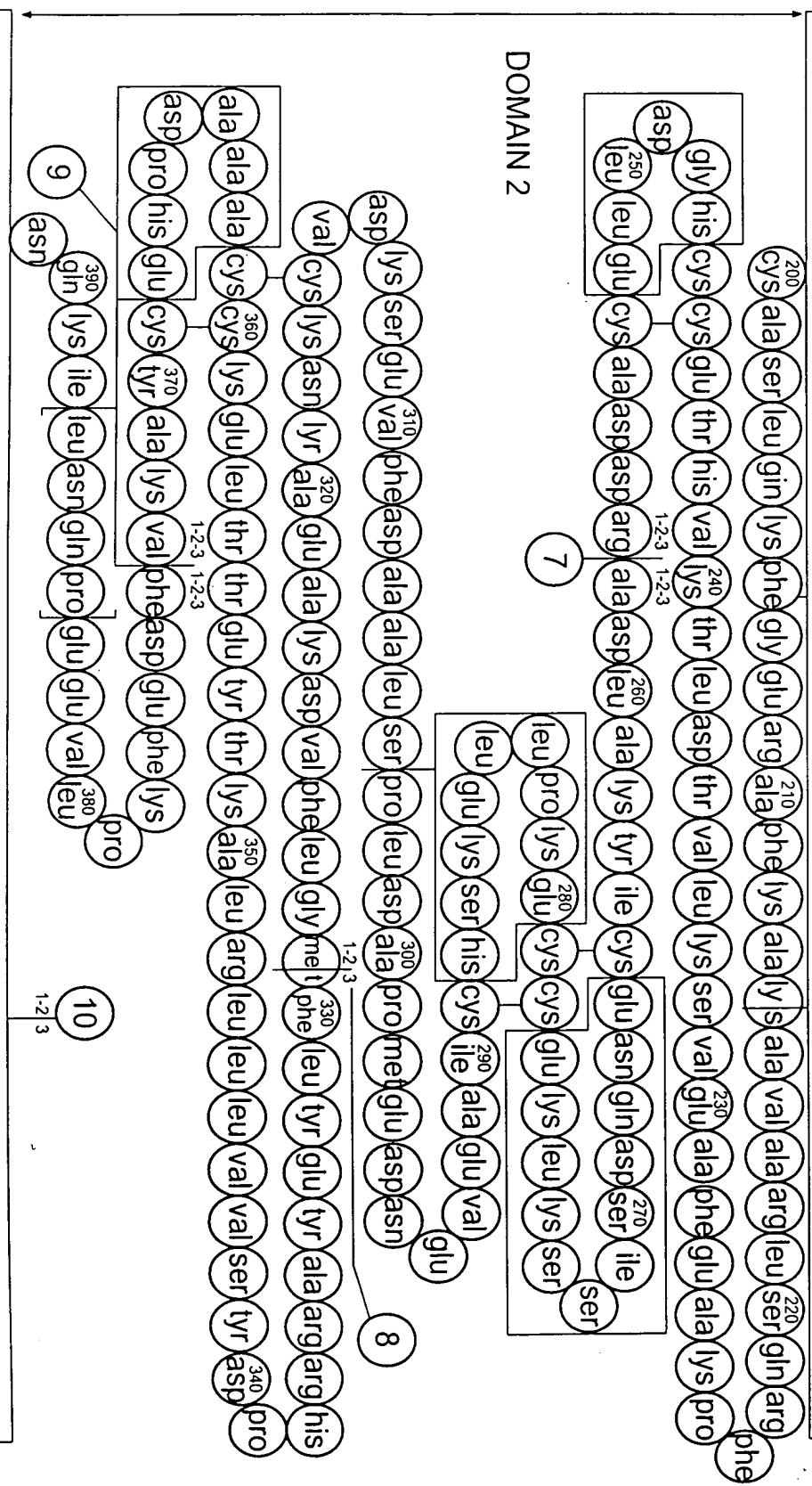


FIG. 11A

TO FIG. 11B

FROM FIG. 11A

FROM FIG. 11A



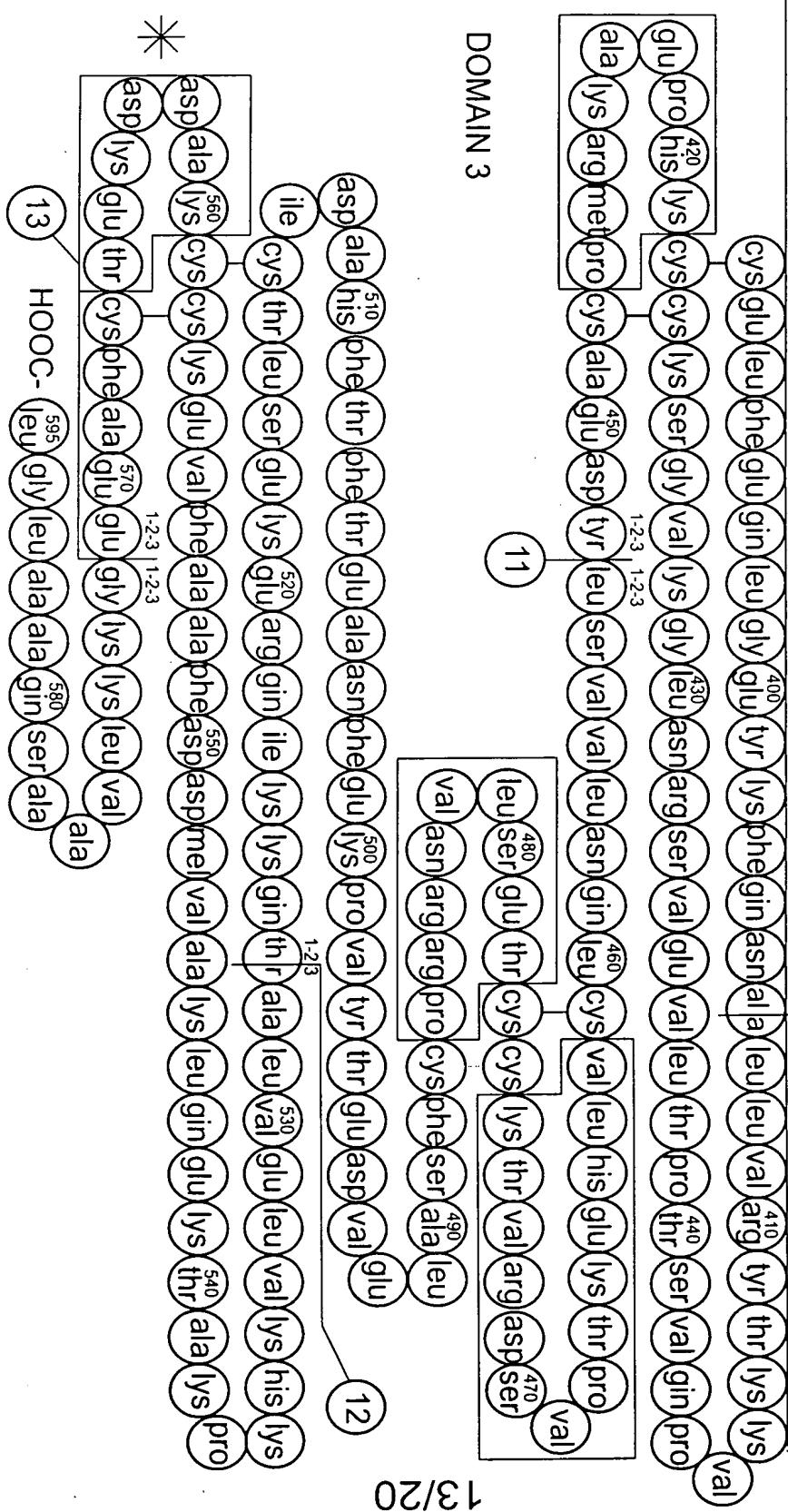
TO FIG. 11C

**FIG. 11B**

TO FIG. 11C

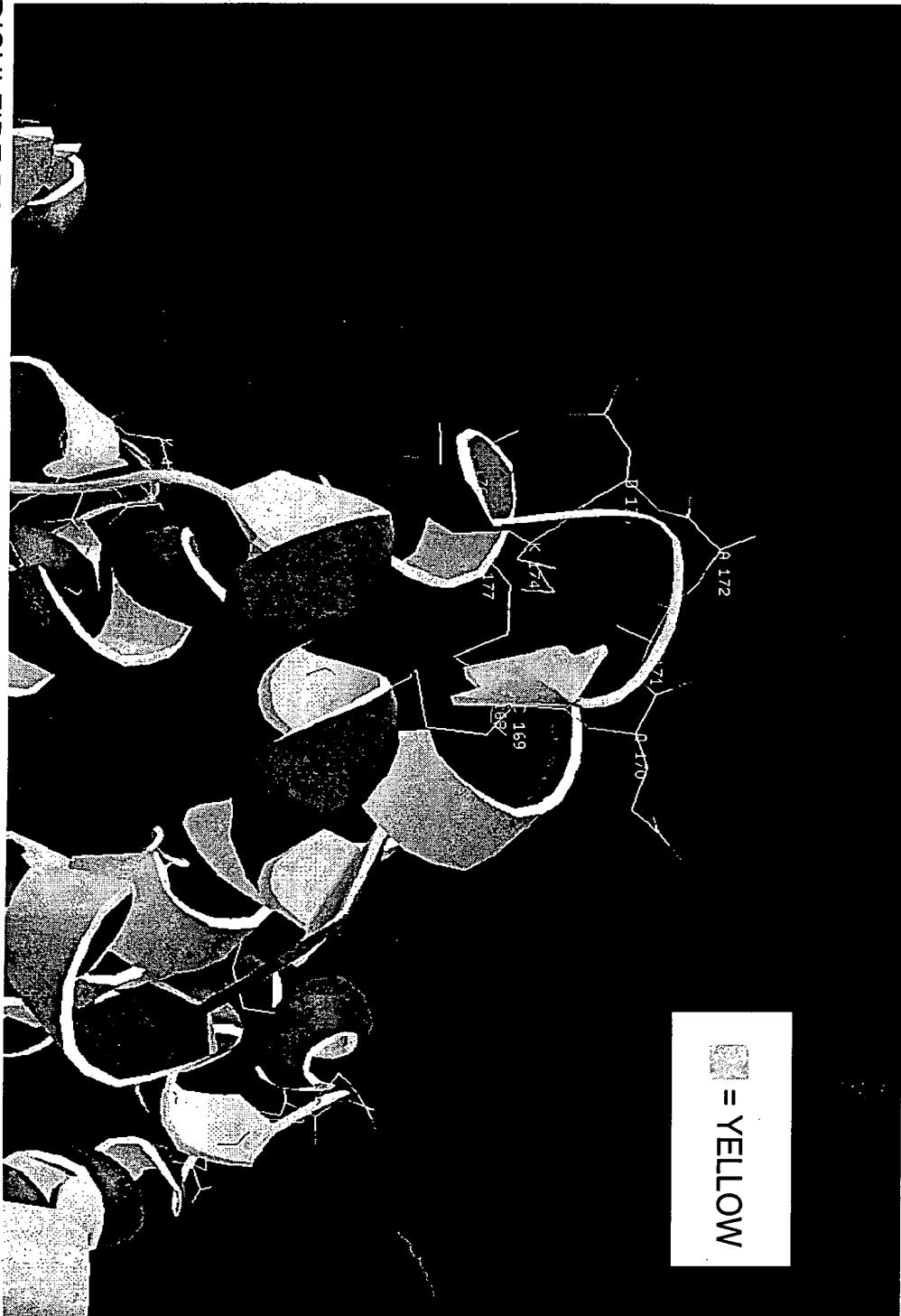
FROM FIG. 11B

FROM FIG. 11B

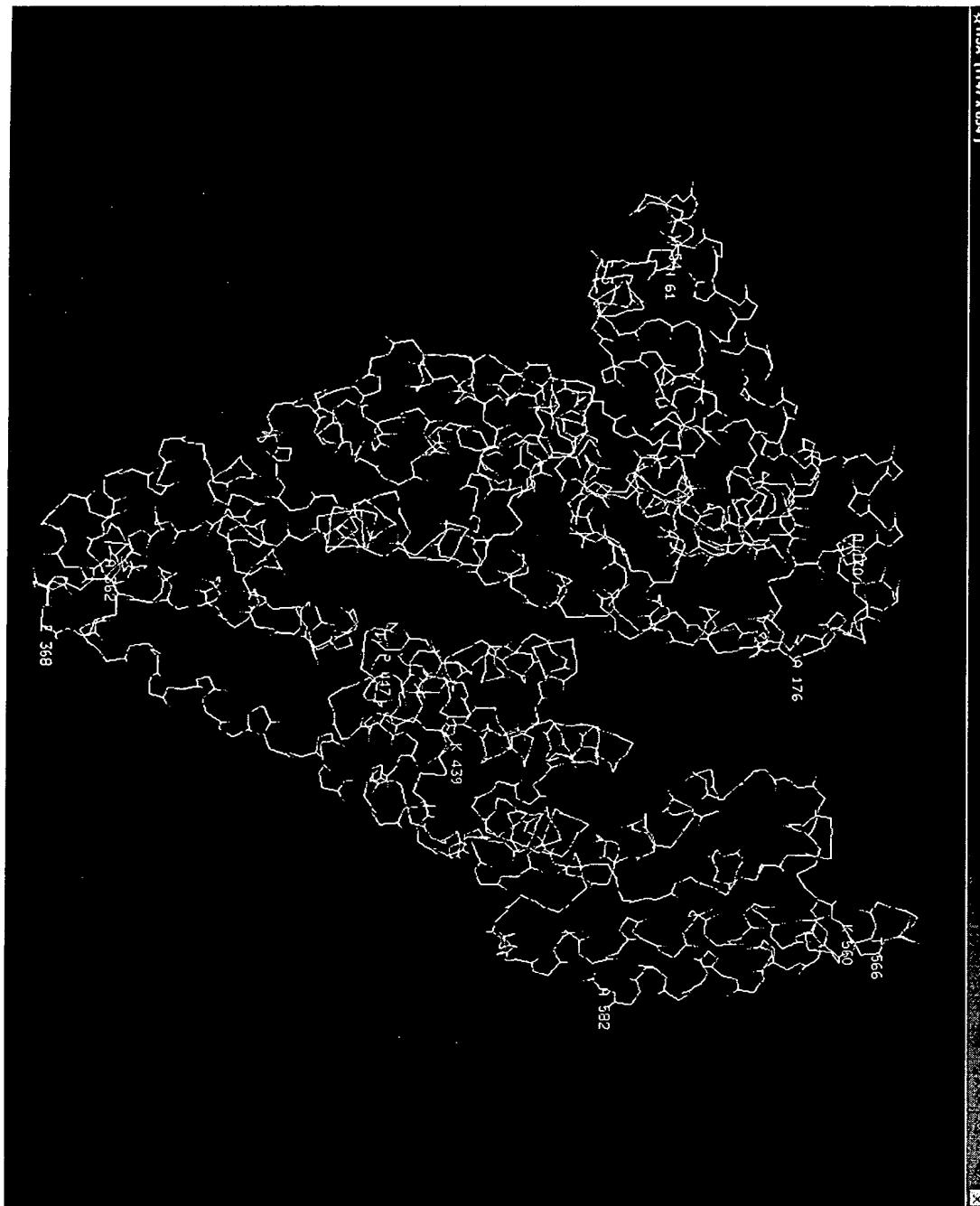


DISULFIDE BONDS SHOWN IN YELLOW

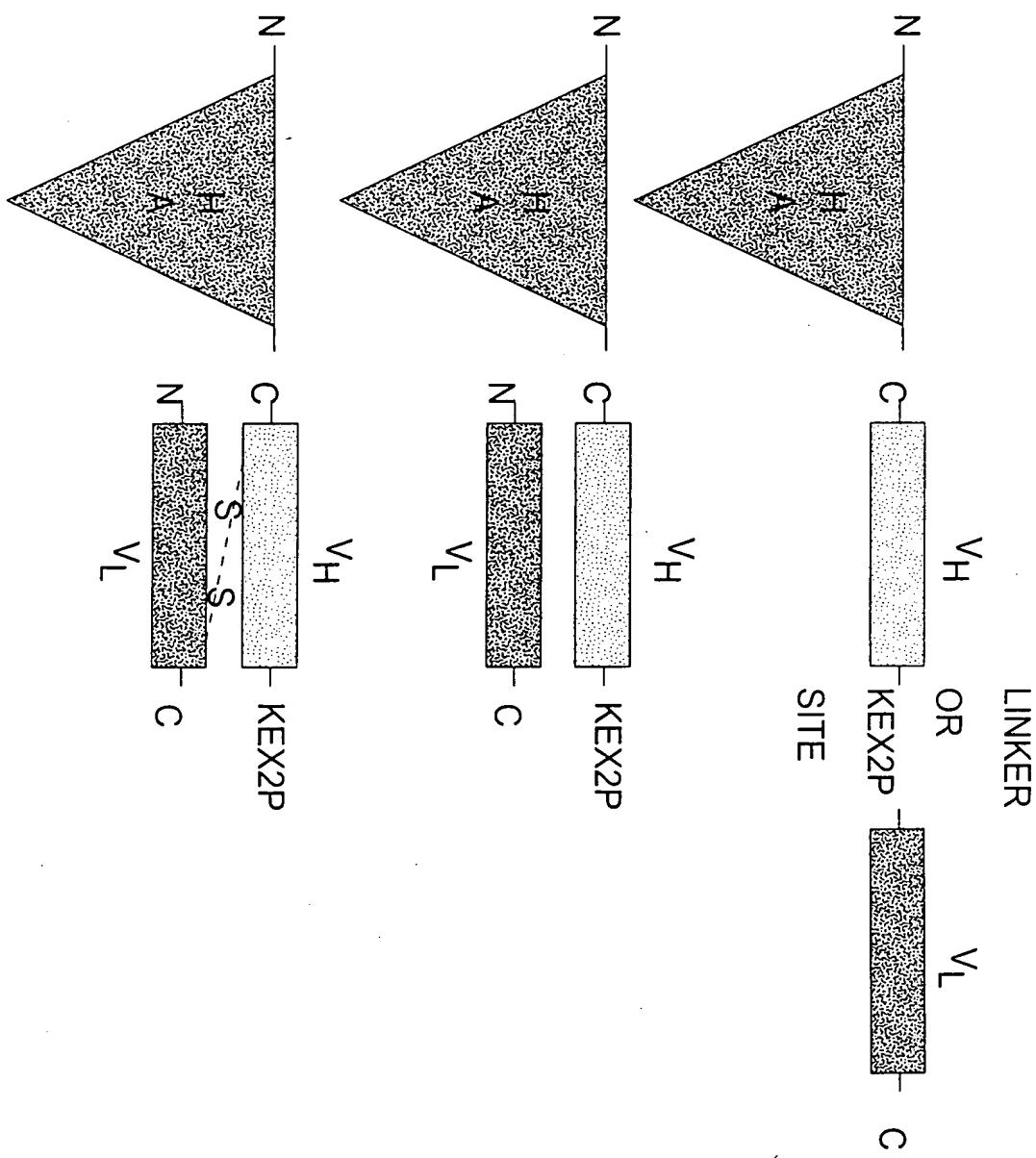
**FIG. 12:**  
*LOOP IV GLU170-A176*



3 HSA (1147 x 894)



**FIG. 13**  
**TERTIARY STRUCTURE OF HA**



**FIG. 14**

1 GAT GCA CAC AAG ACT GAG GTT GCT CAT CGG TTT AAA GAT TTG GGA GAA GAA AAT TTC AAA 60  
1 D A H K S E V A H R F K D L G E E N F K 20  
  
61 GCC TTG GTG TTG ATT GCC TTT GCT CAG TAT CTT CAG CAG TGT CCA TTT GAA GAT CAT GTA 120  
21 A L V L I A F A Q Y L Q Q C P F E D H V 40  
  
121 AAA TTA GTG AAT GAA GTA ACT GAA TTT GCA AAA ACA TGT GTT GCT GAT GAG TCA GCT GAA 180  
41 K L V N E V T E F A K T C V A D E S A E 60  
  
181 AAT TGT GAC AAA TCA CTT CAT ACC CTT TTT GGA GAC AAA TTA TGC ACA GTT GCA ACT CTT 240  
61 N C D K S L H T L F G D K L C T V A T L 80  
  
241 CGT GAA ACC TAT GGT GAA ATG GCT GAC TGC TGT GCA AAA CAA GAA CCT GAG AGA AAT GAA 300  
81 R E T Y G E M A D C C A K Q E P E R N E 100  
  
301 TGC TTC TTG CAA CAC AAA GAT GAC AAC CCA AAC CTC CCC CGA TTG GTG AGA CCA GAG GTT 360  
101 C F L Q H K D D N P N L P R L V R P E V 120  
  
361 GAT GTG ATG TGC ACT GCT TTT CAT GAC AAT GAA GAG ACA TTT TTG AAA AAA TAC TTA TAT 420  
121 D V M C T A F H D N E E T F L K K Y L Y 140  
  
421 GAA ATT GCC AGA AGA CAT CCT TAC TTT TAT GCC CCG GAA CTC CTT TTC TTT GCT AAA AGG 480  
141 E I A R R H P Y F Y A P E L L F A K R 160

Figure 15A

481 TAT AAA GCT GCT TTT ACA GAA TGT TGC CAA GCT GCT GAT AAA GCT GCC TGC CTG TGT CCA 540  
161 Y K A A F T E C C Q A A D K A A C L L P 180  
  
541 AAG CTC GAT GAA CTT CGG GAT GAA GGG AAG GCT TCG TCT GCC AAA CAG AGA CTC AAA TGT 600  
181 K L D E L R D E G K A S S A K Q R L K C 200  
  
601 GCC AGT CTC CAA AAA TTT GGA GAA AGA GCT TTC AAA GCA TGG GCA GTG GCT CGC CTG AGC 660  
201 A S L Q K F G E R A F K A W A V A R L S 220  
  
661 CAG AGA TTT CCC AAA GCT GAG TTT GCA GAA GTT TCC AAG TTA GTG ACA GAT CTT ACC AAA 720  
221 Q R F P K A E F A E V S K L V T D L T K 240  
  
721 GTC CAC ACG GAA TGC TGC CAT GGA GAT CTG CTT GAA TGT GCT GAT GAC AGG GCG GAC CTT 780  
241 V H T E C C H G D L L E C A D D R A D L 260  
  
781 GCC AAG TAT ATC TGT GAA AAT CAG GAT TCG ATC TCC AGT AAA CTG AAG GAA TGC TGT GAA 840  
261 A K Y I C E N Q D S I S S K L K E C C E 280  
  
841 AAA CCT CTG TTG GAA AAA TCC CAC TGC ATT GCC GAA GTG GAA AAT GAT GAG ATG CCT GCT 900  
281 K P L L E K S H C I A E V E N D E M P A 300  
  
901 GAC TTG CCT TCA TTA GCT GCT GAT TTT GTT GAA AGT AGG GAT GTT TGC AAA AAC TAT GCT 960  
301 D L P S L A A D F V E S K D V C K N Y A 320

**Figure 15B**

961 GAG GCA AAG GAT GTC TTC CTG GCC ATG TTT TTG TAT GAA TAT GCA AGA AGG CAT CCT GAT 1020  
321 E A K D V F L G M F L Y E Y A R R H P D 340

1021 TAC TCT GTC GTG CTG CTG CTG AGA CTT GCC AAG ACA TAT GAA ACC ACT CTA GAG AAG TGC 1080  
341 Y S V V L L R L A K T Y E T T L E K C 360

1081 TGT GCC GCT GCA GAT CCT CAT GAA TGC TAT GCC AAA GTG TTC GAT GAA TTT AAA CCT CTT 1140  
361 C A A D P H E C Y A K V F D E F K P L 380

1141 GTG GAA GAG CCT CAG AAT TTA ATC AAA CAA AAC TGT GAG CTT TTT GAG CAG CTT GGA GAG 1200  
381 V E E P Q N L I K Q N C E L F E Q L G E 400

1201 TAC AAA TTC CAG AAT GCG CTA TTA GTT CGT TAC ACC AAG AAA GTA CCC CAA GTG TCA ACT 1260  
401 Y K F Q N A L L V R Y T K K V P Q V S T 420

1261 CCT GAA GCA AAA AGA ATG CCC TGT GCA GAA GAC TAT CTA TCC GTG GTC CTG AAC CAG TTA 1320  
421 P T L V E V S R N L G K V G S K C C K H 440

1321 CCT GAA GCA AAA AGA ATG CCC TGT GCA GAA GAC TAT CTA TCC GTG GTC CTG AAC CAG TTA 1380  
441 P E A K R M P C A E D Y L S V V L N Q L 460

1381 TGT GTG TTG CAT GAG AAA ACC CCA GTA AGT GAC AGA GTC ACA AAA TGC TGC ACA GAG TCC 1440  
461 C V L H E K T P V S D R V T K C C T E S 480

Figure 15C

1441 TTG GTG AAC AGG CGA CCA TGC TTT TCA GCT CTC GAA GTC GAT GAA ACA TAC GTT CCC AAA 1500  
481 L V N R R P C F S A L E V D E T Y V P K 500  
  
1501 GAG TTT AAT GCT GAA ACA TTC ACC TTC CAT GCA GAT ATA TGC ACA CTT TCT GAG AAG GAG 1560  
501 E F N A E T F T F H A D I C T L S E K E 520  
  
1561 AGA CAA ATC AAG AAA CAA ACT GCA CTT GTT GAG CTT GTG AAA CAC AAC AAG CCC AAG GCA ACA 1620  
521 R Q I K K Q T A L V E L V K H K P K A T 540  
  
1621 AAA GAG CAA CTG AAA GCT GTT ATG GAT GAT TTC GCA GCT TTT GTA GAG AAG TGC TGC AAG 1680  
541 K E Q L K A V M D D F A A F V E K C C K 560  
  
1681 GCT GAC GAT AAG GAG ACC TGC TTT GCC GAG GAG GGT AAA AAA CTT GTT GCT GCA AGT CAA 1740  
561 A D D K E T C F A E E G K K L V A A S Q 580  
  
1741 GCT GCC TTA GGC TTA TAA CAT CTA CAT TTA AAA GCA TCT CAG 1782  
581 A A L G L \* 585

Figure 15D